NEWS RELEASE

Inovio Successfully Develops First DNA-Encoded Monoclonal Antibody (dMAb™) Checkpoint Inhibitor and Demonstrates Tumor Shrinkage in Preclinical Studies

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Advancement highlighted in prestigious AACR journal Cancer Research

PLYMOUTH MEETING, Pa., Oct. 08, 2018 (GLOBE NEWSWIRE) -- Inovio Pharmaceuticals, Inc. (NASDAQ:INO) announced today the successful animal testing of DNA-encoded monoclonal antibodies targeting the immune checkpoint molecule CTLA-4 as published in Cancer Research. The breakthrough preclinical study demonstrated that highly optimized dMAbs targeting mouse CTLA-4 protein can be robustly expressed in vivo, and shrank tumors in mice. More importantly, Inovio's dMAb constructs for anti-human CTLA-4 antibodies ipilimumab (YERVOY®) and tremelimumab, achieved high expression levels in mice (approximately 85µg/ml and 58µg/ml, respectively). These dMAbs exhibited long-term expression with maintenance of serum levels >15µg/ml for over a year.

This research publication is significant because it is the first to report on the use of Inovio dMAb technology to develop novel monoclonal antibody-based therapies targeting checkpoint inhibitors. Inovio is developing additional dMAbs targeting other checkpoint molecules including PD-1. When delivered directly into the body, the genetic instructions provided from the dMAb construct enable the patient's own cells to become the factory which manufactures the therapeutic monoclonal antibody products. Inovio has previously published several papers demonstrating its dMAb product candidate's ability to treat multiple virus targets such as flu, dengue, chikungunya, and HIV.

Laurent Humeau, Ph.D., Inovio's Senior Vice President, Research & Development, said, "Even though conventional monoclonal antibodies represent one of the most successful segments of the biotechnology market, accounting for over $50 billion in sales today, manufacturing complexity and repeated dosing may limit a broader use of this technology. Inovio's dMAb products may improve upon this class using our synthetic design and in vivo production. This newly published study further support that Inovio's potent dMAb platform can be expanded to target cancer. We plan on advancing the first clinical dMAb candidate into the first-in-human study in 2019. Moreover, we expect to form partnerships to advance several dMAb products targeting cancers and infectious diseases."

David B. Weiner, Ph.D., the paper's senior author and the W.W. Smith Charitable Trust Professor in Cancer Research at The Wistar

Institute, said, “Our work provides the first demonstration that we can use synthetic DNA technology to produce checkpoint inhibitor molecules in vivo to impact tumor growth in a preclinical setting. We showed that dMAbs may represent a valuable addition to the cancer immunotherapy toolbox: In our preclinical studies, dMAbs achieved antitumor activity comparable to that of traditional monoclonal antibodies, while being delivered through a simpler formulation that may provide a bridge to expand target populations for checkpoint inhibitors.”

The study highlights that delivery of a synthetic, sequence-optimized DNA plasmid designed to encode anti-mouse CTLA-4 monoclonal antibodies, with the aid of an electroporation device to enhance uptake, resulted in significant and prolonged antibody expression with even a single dose. Importantly, this approach stimulated robust CD8+ T cell infiltration, achieving tumor clearance across multiple mouse tumor models. The researchers then went on to develop human checkpoint inhibitor molecules and demonstrated their production in mice and their ability to stimulate human T cell responses associated with antitumor activity. The study clearly demonstrates how optimized dMAbs encoding the human CPI’s ipilimumab and tremelimumab are potently expressed in vivo and enhance the activation of human effector T cells with the potential to destroy tumors. This strategy provides a novel approach to immune checkpoint therapy, with the potential to expand patient access to this breakthrough immunotherapy to treat cancer.

Funded with over $60 million in R&D support from top agencies like DARPA, NIH, and the Gates Foundation, Inovio dMAb products could extend the medical benefits that marketed monoclonal antibodies have already achieved, and even potentially address diseases that conventional monoclonal antibodies cannot.

About Inovio’s DNA-based Monoclonal Antibody Platform

Traditional monoclonal antibodies are manufactured outside the body in bioreactors, typically requiring costly large-scale manufacturing facility development and laborious production. Inovio’s disruptive dMAb technology has the potential to overcome these limitations by virtue of their simplified design, rapidity of development, product stability, ease of manufacturing and deplorability, and cost effectiveness, thereby providing potential new avenues for treating a range of diseases. Another significant advancement seen in Inovio dMAb technologies is that the optimized genes for a desired monoclonal antibody is encoded in a DNA plasmid, which is produced using very cost effective and highly scalable fermentation techniques. These plasmids are delivered directly into cells of the body using electroporation and the encoded monoclonal antibody is then directly produced by these cells. Previously published studies show that a single administration of a highly optimized DNA-based monoclonal antibody targeting HIV virus produced a high level of expression of the antibody in the bloodstream of mice; Inovio similarly reported data showing that dMAb products against flu, Ebola, chikungunya and dengue protected animals against lethal challenge. Inovio Ebola dMAb™ product is being developed under a grant from the Defense Advanced Research Projects Agency (DARPA).

About Inovio Pharmaceuticals, Inc.

Inovio is a late-stage biotechnology company focused on the discovery, development, and commercialization of DNA

immunotherapies that transform the treatment of cancer and infectious diseases. Inovio's proprietary platform technology applies next-generation antigen sequencing and DNA delivery to activate potent immune responses to targeted diseases. The technology functions exclusively in vivo, and has been demonstrated to consistently activate robust and fully functional T cell and antibody responses against targeted cancers and pathogens. Inovio is the only immunotherapy company that has reported generating T cells whose killing capacity correlates with relevant clinical outcomes. Inovio's most advanced clinical program, VGX-3100, is in Phase 3 for the treatment of HPV-related cervical pre-cancer. Also in development are Phase 2 immuno-oncology programs targeting head and neck cancer, bladder cancer, and glioblastoma, as well as platform development programs in hepatitis B, Zika, Ebola, MERS, and HIV. Partners and collaborators include MedImmune, Regeneron, Roche/Genentech, ApolloBio Corporation, The Wistar Institute, University of Pennsylvania, Parker Institute for Cancer Immunotherapy, CEPI, DARPA, GeneOne Life Science, Plumbline Life Sciences, Drexel University, NIH, HIV Vaccines Trial Network, National Cancer Institute, U.S. Military HIV Research Program, and Laval University. For more information, visit **www.inovio.com**.

This press release contains certain forward-looking statements relating to our business, including our plans to develop electroporation-based drug and gene delivery technologies and DNA vaccines, our expectations regarding our research and development programs, including the planned initiation and conduct of clinical trials and the availability and timing of data from those trials, and our plans and expectations regarding partnerships. Actual events or results may differ from the expectations set forth herein as a result of a number of factors, including uncertainties inherent in pre-clinical studies, clinical trials and product development programs, the availability of funding to support continuing research and studies in an effort to prove safety and efficacy of electroporation technology as a delivery mechanism or develop viable DNA vaccines, our ability to support our pipeline of SynCon® active immunotherapy and vaccine products, the ability of our collaborators to attain development and commercial milestones for products we license and product sales that will enable us to receive future payments and royalties, the adequacy of our capital resources, the availability or potential availability of alternative therapies or treatments for the conditions targeted by us or our collaborators, including alternatives that may be more efficacious or cost effective than any therapy or treatment that we and our collaborators hope to develop, issues involving product liability, issues involving patents and whether they or licenses to them will provide us with meaningful protection from others using the covered technologies, whether such proprietary rights are enforceable or defensible or infringe or allegedly infringe on rights of others or can withstand claims of invalidity and whether we can finance or devote other significant resources that may be necessary to prosecute, protect or defend them, the level of corporate expenditures, assessments of our technology by potential corporate or other partners or collaborators, capital market conditions, the impact of government healthcare proposals and other factors set forth in our Annual Report on Form 10-K for the year ended December 31, 2017, our Quarterly Report on Form 10-Q for the quarter ended June 30, 2018 and other regulatory filings we make from time to time. There can be no assurance that any product candidate in our pipeline will be successfully developed, manufactured or commercialized, that final results of clinical trials will be supportive of regulatory approvals required to market licensed products, or that any of the forward-looking information provided herein will be proven accurate. Forward-looking statements speak only as of the date of this release, and we undertake no obligation to update or revise these statements, except as may be required by law.

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